Support for the amendment

The amendments are fully supported in the claims as previously pending, and thus do not constitute new matter.

Remarks

1. Claim cancellation

The Applicant hereby cancels non-elected claims 4-6, without prejudice to their re-filing in a subsequent continuing application.

2. Information Disclosure Statement

The patent office appears to be asserting that legible copies of the cited references were not filed with the information disclosure statement. The Applicants herewith are attaching a copy of the return receipt postcard from the response of May 23, 2003, on which the patent office acknowledged receipt of the references cited in the information disclosure statement. Nonetheless, in order to expedite prosecution of the application, the Applicants are herewith submitting a second set of the references cited in the information disclosure statement. The Applicants thus respectfully request that the patent office consider the submitted references and return an initialed copy of the information disclosure statement to the Applicants representative.

3. Rejection under 35 USC 112, first paragraph

The patent office rejected claims 1 and 12-17 under 35 USC 112, first paragraph based on the assertion that the specification does not enable the full scope of the claims. The Applicants traverse this rejection. The patent office has admitted enablement for in vitro methods of reducing cell migration of epithelial-derived cells by contacting the cells with antibodies to domain III of the $\gamma 2$ chain of laminin 5, but asserts that the lack of in vivo examples renders the specification non-enabling. The Applicants traverse this rejection.

According to MPEP 2164.02 (under Section entitled "Correlation: In vitro/In vivo"), "An in vitro or in vivo animal model example in the specification, in effect, constitutes a 'working example' if that example 'correlates' with a disclosed method or claimed invention...In other words, if the art is such that a particular model is recognized as correlating to a specific condition,

then it should be accepted as correlating unless the examiner has evidence that the model does not correlate."

In the present application, as admitted by the patent office, the Applicants have provided examples of in vitro methods for inhibiting migration of epithelial-derived cells using antibodies to domain III of the γ2 chain of laminin 5. The examples utilize the Boyden chamber assay or the Transwell plate assay (see page 31 line 12 to page 32 line 12 and page 35 line 22 to page 36 line 11).

As demonstrated by the attached supporting documents, the Boyden chamber assay and the Transwell plate assay are accepted in the art as being useful for identifying compounds that can inhibit cell migration in vivo. For example, in discussing the Boyden chamber assay, Iwamoto and Sugioka stated:

> "A variety of human tumors have been studied in this system and we find a high correlation between their invasiveness in vitro and their malignant behavior as exhibited in vivo. We have used this in vitro invasion assay to test for factors which might inhibit tumor cell invasion...These data suggest that the assay system described herein can be successfully utilized to study the invasive activity of tumor cells and those factors that may **inhibit** the spread of malignant cells." (Abstract from Adv. Exp. Med. Biol. 1992; 324:141-149)

Similarly, Melchiori et al. used the Boyden chamber assay to identify peptide inhibitors of tumor cell invasiveness in vitro. The authors concluded:

> "This study demonstrates that addition of an excess peptide containing the matrix metalloprotease prosegment inhibitor sequence can **inhibit** invasive activity at the cellular level and suggests that this may be a useful strategy to modulate tumor cell invasiveness in vivo." (Cancer Res. 1992 Apr 15; 52(8):2353-6)

These references demonstrate that it is accepted in the art that a correlation exists between the ability of compounds to inhibit cell migration in the Boyden chamber assay and the ability of the same compounds to inhibit migration of those cell types in vivo. As discussed above, under MPEP § 2164.02, "if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating, unless the examiner has evidence that the model does not correlate." In addition, "the Examiner must also give reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. A rigorous or an invariable

exact correlation is not required," (MPEP § 2164.02). The patent office has provided no evidence of any kind to refute the correlation between compounds inhibiting cell migration in the Boyden chamber assay and/or the Transwell plate assay, and the ability of the compounds to inhibit cell migration in vivo. Given the acceptance of this correlation in the art, as demonstrated by the attached documents, the Applicants respectfully submit that the patent office has not met its burden for establishing non-enablement of the claims.

Thus, the Applicants respectfully request reconsideration and withdrawal of the rejection.

4. Rejection under 35 USC 112, second paragraph

The patent office rejected claims 1 and 12-17 under 35 USC 112, second paragraph based on the assertion that the claims lack essential steps. Specifically, the patent office asserted that there is no contact step. The Applicants have amended the claims to obviate the rejection, and thus respectfully request reconsideration and withdrawal of this rejection.

5. Rejection under 35 USC 102

The patent office rejected claims 1 and 12-17 as being anticipated by Gianelli (1997). Specifically, the patent office asserted that Gianelli teaches the use of monoclonal antibodies against domain III of the γ2 chain of laminin 5 to inhibit the migration of breast epithelial cells. The Applicants traverse this assertion and the accompanying claim rejections.

The patent office specifically recites the following antibodies used by Gianelli as teaching the use of antibodies against domain III of the γ2 chain of laminin 5:

(a) Antibodies against a laminin 5 receptor

(b) Monoclonal antibody CM6

(c) Monoclonal antibody MIG1

Each of these assertions is analyzed below.

(a) Antibodies against a laminin 5 receptor: As stated in the Gianelli reference, the laminin 5 receptor antibody is directed against integrin α3β1 (see page 227, left column, lines 9-13). Clearly, disclosure of the use of antibody against integrin α3β1 is not a disclosure of the use of an antibody against domain III of the γ2 chain of laminin 5.

(b) Monoclonal antibody CM6: As expressly stated in the Gianelli reference, the CM6 monoclonal antibody is directed to the cell adhesion site of laminin 5 (page 227, left column, lines 18-22). Thus, Gianellli does not teach that the CM6 monoclonal antibody is directed against domain III of the γ2 chain of laminin 5.

(c) Monoclonal antibody MIG1: As expressly stated in the Gianelli reference, the MIG1 monoclonal antibody is directed to the α3 subunit of laminin 5 (page 227, left column, lines 23-28). Clearly, disclosure of the use of antibody against the α3 subunit of laminin 5 is not a disclosure of the use of an antibody against domain III of the γ2 chain of laminin 5.

Thus, the Gianelli reference clearly does not teach the use of antibodies against domain III of the γ2 chain of laminin 5 to reduce epithelial-derived cell migration, as asserted by the patent office. Nor does Gianelli provide any suggestion or motivation to one of skill in the art to use antibodies against domain III of the γ2 chain of laminin 5 to reduce epithelial-derived cell migration.

Based on all of the above, the Applicants respectfully request reconsideration and withdrawal of this rejection.

CONCLUSIONS

Based upon the above amendments and arguments, the Applicant respectfully submits that the claims are ready for allowance. If the Examiner believes that a telephone or personal interview would expedite prosecution of the instant application, the Examiner is invited to call the undersigned attorney at (312) 913-2106.

Respectfully submitted,
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Date: 11/7/03

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